REMARKS

Applicants have amended the claims to more particularly define the invention taking into consideration the outstanding Official Action. Applicants appreciate the courtesy of the interview extended to the undersigned attorney by the Examiner on May 2, 2007 at which time the outstanding rejections were discussed. Applicants have amended claim 1 in accordance with the Examiner's suggestion to overcome the 112 rejection in the outstanding Official Action and at the interview. Applicants note that the objections to the drawings and specification have been withdrawn in light of the reply filed on October 30, 2006. Applicants further note that information disclosure statement filed on October 30, 2006 has been considered.

The rejection of claims 1-7 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention has been carefully considered but is most respectfully traversed in view of the amendments to the claims. Applicants have amended claim 1 in accordance to the Examiner's helpful suggestion indicated in the interview summary of May 2, 2007.

Amended claim 1 has been clarified by inserting a) and b) in front of the two components forming the mixed SAM. The difference between these components is that in a) there is only (OEG) -terminated amide group-containing alkyl thiols and in b) there is (OEG) -terminated amide group-containing alkyl thiols coupled to antigens via amide-group formation. Both a) and b) are firmly attached to the metal surface via their respective thiol-end. Both in a) and b) the alkyl portion of the molecule has 1 -20 methylene groups and the OEG portion of the molecule has 1-15 ethylene oxy units. The antigens in b) are reversibly bound to antibodies. (These antibodies will be displaced in case their antigens are present in a test solution).

The last paragraph of the present specification, page 3, explains that the low molecular weight antigens are synthetically bound to the OEG molecules prior to SAM formation by reacting functional groups on the antigens with functional groups terminating the OEG alkyl thiol. On page 7, lines 7-10 is described: A mixed monolayer

was produced that contained two kinds of molecules, the first being protein repellent and the second being a TNT-analogue, thereby making it possible to obtain SAMs containing a varying amount of analogue that displays low levels of non-specific binding. Accordingly, it is most respectfully requested that the rejection of the claims as indefinite under 35 U.S.C. 112 be withdrawn.

Applicants most respectfully submit that all the claims now present in the application are in full compliance with 35 U.S.C. 112 and are clearly patentable over the references of record.

The rejection of claims 1, 2, 6 and 7 under 35 U.S.C. 103(a) as being unpatentable over Willner et al. in view of Svedhem et al. and Bentley has been carefully considered but is most respectfully traversed in view of the amendments to the claims, the comments already of record and the following comments.

As previously noted, the Willner reference discloses the formation of cystamine monolayer on a gold electrode (page 23, lines 14-24 and Fig. 4). As is evident from Fig. 4, the monolayer is first formed and thereafter the antigen is added so that an antigen-cystamine monolayer immobolized on the electrode is obtained (page 4, lines 2-3). In this Willner reference, there is no suggestion of any other "capturing agent" than cystamine, only a very non-specific mentioning of a sulfur containing moiety as the capturing agents is mentioned on page 14, lines 22-23. There is no discussion of any possible effects of the "capturing agent" in the Willner reference, and therefore there is no motivation for one of ordinary skill in the art to modify said "capturing agent". This position is reiterated since the outstanding rejection does not provide the necessary motivation to provide the results as achieved in the presently claimed invention.

Applicants most respectfully submit that although the Svedham reference is similar to the present invention, Svedhem et al, however, produce SAMs with planar biosensing interfaces for possible subsequent interaction with large entities such as phages or cells. (see page 4494, right column, lines 5 and last sentence of the first passage).

Thus, the Svedhem references does neither discloses nor suggests a mixed SAM of two different molecules, one of which contains an antigen and a reversibly

bound antibody ready for displacement reactions with analyte antigens in accordance with the presently claimed invention. Further, there is no indication of success in forming SAM monolayers of non-identical starting compounds. The teaching of this reference does not overcome the deficiencies of the primary reference.

The Svedham reference describes two step procedures for obtaining a SAM with biologically active molecules. First a SAM is produced and then an amine derivative is surface coupled to carboxylate SAMs (see page 4495, left column, lines 6,7). On the same page, right column lines 12 -15, there is the disclosure that "A carboxylic acid group terminated analogue (6) has been included with which functionality for coupling of biomolecules of interest can be introduced into the monolayer[17]." Applicants submit herewith an abstract of reference 17 found at www.pubmed.gov (J. Lahiri, et al., "A strategy for the generation of surfaces presenting ligands of studies of binding based on an active ester as a common reactive intermediate: a surface plasm on resonance", Anal Chem, Feb. 15, 1999, vol. 71, no. 4), which describes the preparation of a mixed SAM of molecules of different lengths, wherein one type of molecule terminated with -OH and the other type of molecule is terminated with $-OCH_2COOH$. Then reactive N-hydroxylsuccinimidyl ester were created from the carboxylic acid endgroups and finally these were coupled to amines on a protein or ligand on the pre-formed SAM surface.

The Svedhem reference does not comprise any disclosure or suggestion of producing a SAM from two types of molecules, where one type of molecule is already coupled to a bioactive group as in the present invention. Please note that the amended claim 1 states that the coating consists of the molecules a) and b). Thus the coating does not comprise unreacted reactive groups but rather an "inert molecule" and a "biologically active molecule" only. This is in contrast to the disclosures in the Svedhem reference and reference 17 cited therein since chemical reactions do not produce only the desired coupling of two molecules in a solution with reactants. Some of the activated (e.g. N-hydroxylsuccinimidyl activated carboxylic acid endgroups) will be hydrolyzed or react in an unwanted direction) and there will always be an excess of one or the other reaction components. Therefore, the prior art will inevitably have activated carboxylic groups that will be hydrolyzed in the final product since there is no possibility

to fully control attachment of the proteins or ligands to all activated carboxylic groups. From product control point of view, the present invention provides well defined mixed SAMs comprising a known amount of attached biomolecules whereas the prior art produces less well defined mixed SAMs comprising at best an approximately known amount of attached biomolecules. The teachings of the Bentley reference does not overcome the deficiencies of the primary references for reason previously of record.

In summary, most prior art is concerned with planar surfaces of SAMs, which may be of mixed SAMs, but the SAMs already exist when they are used for binding bioactive ligands to the surfaces. In the present invention, the bioactive molecule is coupled to one of two SAM-forming molecules prior to the formation of a SAM. The products of the invention are therefore not contaminated by non-reacted reactive groups and hydrolyzed products. The cited Willner et al reference does not disclose SAMs, nor does Bentley et al. Accordingly, it is most respectfully requested that this rejection be withdrawn.

Applicants would like to bring to the Examiner's attention that, just before the filing of the priority application, US provisional application 60/389,497 filed on June 19, 2002, professor Bo LIEDBERG, who is an inventor to the present invention, published a paper with other authors entitled "Synthesis and Self-Assembly of Globotriose Derivatives: A Model System for Studies of Carbohydrate-Protein Interactions", Langmuir, 2002, vol. 18, pp. 2848-2858, which is submitted herewith. Disclosed is the production of mixed SAMs from two different molecules, one of which is coupled to a carbohydrate. The carbohydrate is said to bind to antibodies. In the present invention, the antigen, coupled to one of two SAM forming molecules, is selected from the group consisting of optionally derivatized explosives and narcotics and is reversibly bound to an antibody specific for the antigen. Explosives and narcotics are not carbohydrates, and there is no disclosure or suggestion in said paper, nor in prior art, of the possibility to obtain mixed SAM surfaces with a controlled amount of defined antigens reversible bound to antibodies as in the present invention.

The rejection of claims 3-5 under 35 U.S.C. 103(a) as being unpatentable over Willner in view of Svedham and Bentley as applied to claim 1 above and further in view

of Duffy has been carefully considered but is most respectfully traversed in view of the above comments and those already of record. While Applicants appreciate that Duffy discloses arrays or patches for biomolecule binding, this reference does not disclose displacement reactions nor the formation of mixed molecules in the SAM. Accordingly, it does not overcome the deficiencies of the primary references and therefore it is most respectfully requested that this rejection be withdrawn.

In view of the above comments and further amendments to the claims, favorable reconsideration and allowance of all the claims now present in the application are most respectfully requested.

Respectfully submitted,
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